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* * * * * * * * * * * * * * * Welcome to STN International * * * * * * * * * * *

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NEWS 3 Jun 03 New e-mail delivery for search results now available
NEWS 4 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
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NEWS 8 Sep 16 Experimental properties added to the REGISTRY file
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 10 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
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NEWS 16 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17 Dec 17 TOXCENTER enhanced with additional content
NEWS 18 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 19 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
ENERGY, INSPEC
NEWS 20 Feb 13 CANCERLIT is no longer being updated
NEWS 21 Feb 24 METADEX enhancements
NEWS 22 Feb 24 PCTGEN now available on STN
NEWS 23 Feb 24 TEMA now available on STN
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 25 Feb 26 PCTFULL now contains images
NEWS 26 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27 Mar 20 EVENTLINE will be removed from STN
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NEWS 29 Mar 24 Additional information for trade-named substances without
structures available in REGISTRY
NEWS 30 Apr 11 Display formats in DGENE enhanced
NEWS 31 Apr 14 MEDLINE Reload
NEWS 32 Apr 17 Polymer searching in REGISTRY enhanced
NEWS 33 Jun 13 Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34 Apr 21 New current-awareness alert (SDI) frequency in
WPIDS/WPINDEX/WPIX
NEWS 35 Apr 28 RDISCLOSURE now available on STN
NEWS 36 May 05 Pharmacokinetic information and systematic chemical names
added to PHAR
NEWS 37 May 15 MEDLINE file segment of TOXCENTER reloaded
NEWS 38 May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39 May 16 CHEMREACT will be removed from STN
NEWS 40 May 19 Simultaneous left and right truncation added to WSCA
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and
right truncation
NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB
NEWS 43 Jun 06 PASCAL enhanced with additional data
NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available

NEWS 45 Jun 25 HSDB has been reloaded

| | |
|--------------|---|
| NEWS EXPRESS | April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003 |
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STRUCTURE FILE UPDATES: 4 JUL 2003 HIGHEST RN 542812-68-0
DICTIONARY FILE UPDATES: 4 JUL 2003 HIGHEST RN 542812-68-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

```

=> s 'gly-pro-arg-pro-pro'/sqefp
      128 'GLY''PRO''ARG''PRO''PRO'/SQEFP
      53435 SQL=5
L1      128 'GLY-PRO-ARG-PRO-PRO'/SQEFP
          ('GLY''PRO''ARG''PRO''PRO'/SQEFP AND SQL=5)

=> s 'gly-ala-gly-gly'/sqefp
      2063 'GLY''ALA''GLY''GLY'/SQEFP
      55928 SQL=4
L2      2063 'GLY-ALA-GLY-GLY'/SQEFP
          ('GLY''ALA''GLY''GLY'/SQEFP AND SQL=4)

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=> s 'gly-pro-arg'/sqefp
      150 'GLY''PRO''ARG'/SQEFP
      1450 SQL=3
L3      150 'GLY-PRO-ARG'/SQEFP
          ('GLY''PRO''ARG'/SQEFP AND SQL=3)
```

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=> fil .search
COST IN U.S. DOLLARS           SINCE FILE        TOTAL
                                ENTRY          SESSION
FULL ESTIMATED COST          20.10          20.94
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FILE 'MEDLINE' ENTERED AT 09:00:03 ON 07 JUL 2003

FILE 'CAPLUS' ENTERED AT 09:00:03 ON 07 JUL 2003
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FILE 'BIOSIS' ENTERED AT 09:00:03 ON 07 JUL 2003
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FILE 'USPATFULL' ENTERED AT 09:00:03 ON 07 JUL 2003
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FILE 'EMBASE' ENTERED AT 09:00:03 ON 07 JUL 2003
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=> d his

(FILE 'HOME' ENTERED AT 08:55:51 ON 07 JUL 2003)

FILE 'REGISTRY' ENTERED AT 08:57:59 ON 07 JUL 2003
L1 128 S 'GLY-PRO-ARG-PRO-PRO'/SQEFP
L2 2063 S 'GLY-ALA-GLY-GLY'/SQEFP
L3 150 S 'GLY-PRO-ARG'/SQEFP

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 09:00:03 ON
07 JUL 2003,

=> s l3 and l1
L4 1 L3 AND L1

=> d ibib ab

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996331937 CAPLUS
DOCUMENT NUMBER: 125:79699
TITLE: Synthetic collagen-like domain derived from the macrophage scavenger receptor binds acetylated low-density lipoprotein in vitro
AUTHOR(S): Tanaka, Toshiaki; Nishikawa, Akeni; Tanaka, Yuji; Nakamura, Haruki; Kodama, Tatsuhiro; Imanishi, Takeshi;
Doi, Takefumi
CORPORATE SOURCE: Protein Eng. Res. Inst., Osaka, 565, Japan
SOURCE: Protein Engineering (1996), 9(3), 307-313
CODEN: PRENE9; ISSN: 0269-2139
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bovine macrophage scavenger receptor is a 70 kDa membrane protein that is trimerized on the macrophage cell surface. The receptor binds modified low-d. lipoproteins (LDL). The core binding site is located within 22 residues at the C-terminus of the collagen-like domain of the receptor. The Lys residue at position 337 plays an important role in ligand binding. Here, the collagen-like domain was constructed using a peptide architecture technique, in which three collagenous peptide chains were crosslinked at their N-termini. The crosslinked peptide showed a collagen-like structure by CD and existed mainly in a monomeric triple helical form as shown by gel exclusion chromatog. The triple-stranded peptide was demonstrated to bind acetylated LDL (Ac-LDL) using regions derived from Gly323 to Lys340 of the natural bovine scavenger receptor. However, a single-stranded peptide with the same amino acid sequence did not bind Ac-LDL. Furthermore, a triple-stranded mutated peptide in which Lys corresponding to Lys337 in the mother protein was substituted with Ala showed no binding activity to Ac-LDL. These results, taken together, indicate that the synthetic collagen-like peptide has a similar structure to the binding site in the scavenger receptor, and support the view that the collagen-like domain of the natural scavenger receptor recognizes Ac-LDL.

<C

09/763,777. Page 5

=> s 14 and (chelat? or ligand?)
L5 1 L4 AND (CHELAT? OR LIGAND?)

=> s 15 and (radiolabel? or label? or radionuclid? or radioisotop? or radioactiv?)
L6 0 L5 AND (RADIOLABEL? OR LABEL? OR RADIONUCLID? OR RADIOISOTOP?
OR RADIOACTIV?)

=> s 13 and 12
L7 7 L3 AND L2

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 6 DUP REM L7 (1 DUPLICATE REMOVED)

=> d ibib ab 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003:300424 CAPLUS
 DOCUMENT NUMBER: 138:316887
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic thioethers
 INVENTOR(S): Cyr, John E.; Pearson, Daniel A.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl. No. PCT/US01/50423.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2003072709 | A1 | 20030417 | US 2003-131543 | 20020424 |
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: US 2000-694992 A2 20001024
WO 2001-US50423 A2 20011024
US 2000-695360 A1 20001024
US 2000-695494 A1 20001024 | | | | |

OTHER SOURCE(S): MARPAT 138:316887
 AB Radiopharmaceutical compns. which are stabilized by addn. of a hydrophilic thioether (Markush structures are included).

L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003:435053 CAPLUS
 DOCUMENT NUMBER: 139:12393
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic 6-hydroxychromans
 INVENTOR(S): Cyr, John E.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of Appl. No. PCT/US01/50423.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2003103899 | A1 | 20030605 | US 2002-131346 | 20020424 |
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: US 2000-695360 A2 20001024
WO 2001-US50423 A2 20011024
US 2000-694992 A1 20001024
US 2000-695494 A1 20001024 | | | | |

AB A compn. comprising a peptide or non-peptide radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic 6-hydroxychroman deriv., e.g., 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox), is described. A kit comprising a sealed vial contg. a predetd. quantity of

a radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic 6-hydroxychroman deriv. is also described. For example, Trolox increased the radiolabeling yield and the stability of ^{99m}Tc depreotide prepnd. from the kit.

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003:435052 CAPLUS
 DOCUMENT NUMBER: 139:12392
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic thioethers and hydrophilic 6-hydroxychromans
 INVENTOR(S): Cyr, John E.; Pearson, Daniel A.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of Appl. No. PCT/US01/50423.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2003103895 | A1 | 20030605 | US 2002-131546 | 20020424 |
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: US 2000-695494 A2 20001024
WO 2001-US50423 A2 20011024
US 2000-694992 A1 20001024
US 2000-695360 A1 20001024 | | | | |

AB A compn. contg. a peptide or non-peptide radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic thioether and a hydrophilic 6-hydroxychroman deriv. The thioether is selected from, e.g., methionine, ethionine, 3-(methylthio)propionaldehyde, 2-(ethylthio)ethylamine, buthionine, S-methyl-cysteine, and methioninol. The hydrophilic 6-hydroxychroman used is, e.g., 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid or 6-hydroxy-2,5,7,8-tetramethylchroman-2-glucosamine. A kit comprising a sealed vial contg.

a predetd. quantity of a radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic thioether and a hydrophilic 6-hydroxychroman deriv. is also described. For example, the combination of L-methionine and Trolox increased the radiolabeling yield and the stability of ^{99m}Tc depreotide prepnd. from the kit.

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:594711 CAPLUS
 DOCUMENT NUMBER: 137:159312
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic thioethers and hydrophilic 6-hydroxychromans
 INVENTOR(S): Cyr, John E.; Pearson, Daniel A.
 PATENT ASSIGNEE(S): Distide, Inc., USA
 SOURCE: PCT Int. Appl., 64 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003072709 | A1 | 20030417 | US 2002-131543 | 20020424 |
| US 2003103899 | A1 | 20030605 | US 2002-131346 | 20020424 |
| US 2003103895 | A1 | 20030605 | US 2002-131546 | 20020424 |
| PRIORITY APPLN. INFO.: US 2000-694992 A1 20001024
US 2000-695360 A1 20001024
US 2000-695494 A1 20001024
WO 2001-US50423 A2 20011024 | | | | |

AB Radiopharmaceutical compns. which are stabilized by addn. of a hydrophilic thioether, a hydrophilic 6-hydroxy-chroman deriv., or a mixt. of a hydrophilic thioether and a hydrophilic 6-hydroxy-chroman deriv. are described. Several examples are provided demonstrating the stabilizing effects of L-methionine, Trolox, or a combination of the two on lyophilized kit preps. contg. ^{99m}Tc-labeled depreotide, benzodiazepinedione deriv., a glycoprotein IIb/IIIa receptor-binding peptide, a peptide chelator, a bisamine bisthiol chelator, or other peptides.

L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002-694638 CAPLUS
 DOCUMENT NUMBER: 137-366262

TITLE: Inhibition of adhesion of type 1 fimbriated *Escherichia coli* to highly mannosylated ligands
 AUTHOR(S): Nagahori, Noriko; Lee, Reiko T.; Nishimura, Shin-Ichiro; Page, Daniel; Roy, Rene; Yuan C.
 CORPORATE SOURCE: Laboratory of Inorganic Chemistry & Glycoclusters,
 Division of Biological Sciences, Graduate School of
 Science, Hokkaido University, Sapporo, 060-0810,

Japan
 SOURCE: ChemBioChem (2002), 3(9), 836-844
 CODEN: CBCHFK; ISSN: 1439-4227

PUBLISHER: Wiley-VCH Verlag GmbH
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB The inhibitory potencies of a no. of mannosides, di- and trivalent mannosides, a set of mannose-terminating dendrimers, and five types of mannose-bearing neoglycoproteins were determined by using a binding assay that measures the binding of ¹²⁵I-labeled, highly mannosylated neoglycoprotein to a type 1 fimbriated *Escherichia coli* (K12) strain in suspension. The IC₅₀ values (the concn. of inhibitor that causes 50% redn. in the bound ¹²⁵I-ligand to *E. coli*) obtained by this method were much lower than the equiv. values obtained by hemagglutination or in assays that involve microplate immobilization. Two important factors that strongly influence the affinity to *E. coli* adhesin are: 1) the presence of an alpha-oriented aglycon that has a long aliph. chain or an arom. group immediately next to the glycosyl oxygen, and 2) the presence of multiple mannose residues that can span a distance of 20 nm or longer on a relatively inflexible structure. The two best inhibitors, which are a highly mannosylated neoglycoprotein with the longest linking arm between

a mannose and protein amino group and the largest mannosylated dendrimer (fourth generation), exhibited sub-nM IC₅₀ values.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1995-837362 CAPLUS
 DOCUMENT NUMBER: 124:56665

TITLE: Design of metal ion binding peptides
 AUTHOR(S): Fattorusso, R.; Morelli, G.; Lombardi, A.; Nastri, F.;

CORPORATE SOURCE: Maglio, O.; D'Auria, G.; Pedone, C.; Pavone, V.
 Res. Cent. Bioactive Peptides, Univ. Naples Federico II, Naples, 80134, Italy
 SOURCE: Biopolymers (1995), 37(6), 401-10
 CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: Wiley
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Two cyclic and branched peptides (PLA and AZU) were synthesized with the aim of reproducing the active site of the blue copper proteins plastocyanin and azurin. Both peptides, designed on the basis of the X-ray structures of Poplar plastocyanin and *Alcaligenes denitrificans* azurin, contain the same coordinating residues of the parent native proteins. The visible spectra of PLA in the presence of equimolar amt. of

Cu(II) strongly support the interaction between the peptide and copper(II) ion. The CD titrn. of AZU with the Hg(II) ion indicates the formation of two species, [AZUHg]⁺ and [AZUHg²⁺]³⁻ having binding consts. (K_{eq}) of 3.106 and 2.104 M⁻¹, resp.

<C

09/763,777. Page 8

=> s l8 and (radionuclid? or radiolabel? or label? or radioisotop? or radioactiv?)
L9 5 L8 AND (RADIONUCLID? OR RADIOLABEL? OR LABEL? OR RADIOISOTOP?
 OR RADIOACTIV?)

=> d ibib ab 1-
YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003-435053 CAPLUS
 DOCUMENT NUMBER: 139:12392
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic 6-hydroxychromans
 INVENTOR(S): Cyr, John E.
 PATENT ASSIGNEE(S): U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of Appl.
 SOURCE: No. PCT/US01/50423.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 2003103899 | A1 | 20030605 | US 2002-131346 | 20020424 |
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2000-695360 | A2 20001024 |
| | | | WO 2001-US50423 | A2 20011024 |
| | | | US 2000-694992 | A1 20001024 |
| | | | US 2000-695494 | A1 20001024 |

AB A compn. comprising a peptide or non-peptide radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic 6-hydroxychroman deriv., e.g., 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox), is described. A kit comprising a sealed vial contg. a predctd. quantity of a radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic 6-hydroxychroman deriv. is also described. For example, Trolox increased the radiolabeling yield and the stability of 99mTc depreotide prepd. from the kit.

a radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic 6-hydroxychroman deriv. is described. For example, Trolox increased the radiolabeling yield and the stability of 99mTc depreotide prepd. from the kit.

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003:300424 CAPLUS
 DOCUMENT NUMBER: 138:316887
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic thioethers
 INVENTOR(S): Cyr, John E.; Pearson, Daniel A.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl.
 No. PCT/US01/50423.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 2003072709 | A1 | 20030417 | US 2002-131543 | 20020424 |
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2000-694992 | A2 20001024 |
| | | | WO 2001-US50423 | A2 20011024 |
| | | | US 2000-695360 | A1 20001024 |
| | | | US 2000-695494 | A1 20001024 |

OTHER SOURCE(S): MARPAT 138:316887
 AB Radiopharmaceutical compns. which are stabilized by addn. of a hydrophilic thioether (Markush structures are included).

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2003-435052 CAPLUS
 DOCUMENT NUMBER: 139:12392
 TITLE: Stabilization of radiopharmaceutical compositions using hydrophilic thioethers and hydrophilic 6-hydroxychromans
 INVENTOR(S): Cyr, John E.; Pearson, Daniel A.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of Appl.
 No. PCT/US01/50423.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 2003103895 | A1 | 20030605 | US 2002-131546 | 20020424 |
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2000-695494 | A2 20001024 |
| | | | WO 2001-US50423 | A2 20011024 |
| | | | US 2000-694992 | A1 20001024 |
| | | | US 2000-695360 | A1 20001024 |

AB A compn. contg. a peptide or non-peptide radiopharmaceutical precursor and a stabilizing amt. of a hydrophilic thioether and a hydrophilic 6-hydroxychroman deriv. is described. The thioether is selected from, e.g., methionine, ethionine, 3-(methylthio)propionaldehyde, 2-(ethylthio)ethylamine, buthionine, S-methyl-cysteine, and methioninol. The hydrophilic 6-hydroxychroman used is, e.g., 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid or 6-hydroxy-2,5,7,8-tetramethylchroman-2-glucosamine. A kit comprising a sealed vial contg.

a predctd. quantity of a radiopharmaceutical precursor and a stabilizing amt. of a mixt. of a hydrophilic thioether and a hydrophilic 6-hydroxychroman deriv. is also described. For example, the combination of L-methionine and Trolox increased the radiolabeling yield and the stability of 99mTc depreotide prepd. from the kit.

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:694638 CAPLUS
 DOCUMENT NUMBER: 137:366262
 TITLE: Inhibition of adhesion of type 1 fimbriated Escherichia coli to highly mannosylated ligands
 AUTHOR(S): Nagahori, Noriko; Lee, Reiko T.; Nishimura, Shin-Ichiro; Page, Daniel; Roy, Rene; Lee, Yuan C.
 CORPORATE SOURCE: Laboratory of Bioorganic Chemistry & Glycoclusters, Division of Biological Sciences, Graduate School of Science, Hokkaido University, Sapporo, 060-0810, Japan
 SOURCE: ChemBioChem (2002), 3(9), 836-844
 CODEN: CBCHX; ISSN: 1439-4227
 PUBLISHER: Wiley-VCH Verlag GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The inhibitory potencies of a no. of mannosides, di- and trivalent mannosides, a set of mannose-terminating dendrimers, and five types of mannose-bearing neoglycoproteins were detd. by using a binding assay that measures the binding of 125I-labeled, highly mannosylated neoglycoprotein to a type 1 fimbriated Escherichia coli (K12) strain in suspension. The IC50 values (the concn. of inhibitor that causes 50% redn. in the bound 125I-ligand to E. coli) obtained by this method were much lower than the equiv. values obtained by hemagglutination or in assays that involve microplate immobilization. Two important factors that strongly influence the affinity to E. coli adhesin are: 1) the presence of an alpha-oriented aglycon that has a long aliph. chain or an arom. group

immediately next to the glycosyl oxygen, and 2) the presence of multiple mannose residues that can span a distance of 20 nm or longer on a relatively inflexible structure. The two best inhibitors, which are a highly mannosylated neoglycoprotein with the longest linking arm between a mannone and protein amino group and the largest mannosylated dendrimer (fourth generation), exhibited sub-nM IC50 values.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

LO ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2004:594711 CAPLUS
 DOCUMENT NUMBER: 1371159312
 TITLE: Stabilization of radiopharmaceutical compositions
 using hydrophilic thioethers and hydrophilic

6-hydroxy

chromane
 INVENTOR(S): Cyr, John E.; Pearson, Daniel A.
 PATENT ASSIGNEE(S): Diatide, Inc., USA
 SOURCE: PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2002060491 | A2 | 20020808 | WO 2001-US50423 | 20011024 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, C2, DE, DK, DM, D2, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, A2, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2003072709 | A1 | 20030417 | US 2002-131542 | 20020424 |
| US 2003103899 | A1 | 20030605 | US 2002-131346 | 20020424 |
| US 2003103895 | A1 | 20030605 | US 2002-131542 | 20020424 |
| PRIORITY APPLN. INFO.: | | | US 2000-694992 | A1 20001024 |
| | | | US 2000-695360 | A1 20001024 |
| | | | US 2000-695494 | A1 20001024 |
| | | | WO 2001-US50423 | A2 20011024 |

AB Radiopharmaceutical compns. which are stabilized by addn. of a hydrophilic thioether, a hydrophilic 6-hydroxy-chroman deriv., or a mixt. of a hydrophilic thioether and a hydrophilic 6-hydroxy-chroman deriv. are described. Several examples are provided demonstrating the stabilizing effects of L-methionine, Trolox, or a combination of the two on lyophilized kit preps. contg. 99mTc-labeled depreotide, benzodiazepinedione deriv., a glycoprotein IIb/IIa receptor-binding peptide, a peptide chelator, a bisamine bishiol chelator, or other peptides.

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09/763,777. Page 11

| | | |
|--|------------------|---------------|
| => FIL STNGUIDE | | |
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
| FULL ESTIMATED COST | 260.32 | 281.26 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -7.81 | -7.81 |

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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Jul 4, 2003 (20030704/UP).

=> s l4 and (radionuclid? or radiolabel? or label? or radioactiv?)
 'SQEFP' IS NOT A VALID FIELD CODE
 0 'GLY-PRO-ARG'/SQEFP
 0 'GLY-PRO-ARG-PRO-PRO'/SQEFP
 1 RADIONUCLID?
 0 RADIOLABEL?
 171 LABEL?
 2 RADIOACTIV?
 L10 0 L4 AND (RADIONUCLID? OR RADIOLABEL? OR LABEL? OR RADIOACTIV?)

| | | |
|--|------------------|---------------|
| => fil .search | | |
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
| FULL ESTIMATED COST | 0.42 | 281.68 |
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| CA SUBSCRIBER PRICE | 0.00 | -7.81 |

FILE 'MEDLINE' ENTERED AT 09:13:08 ON 07 JUL 2003

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FILE 'EMBASE' ENTERED AT 09:13:08 ON 07 JUL 2003
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=> s l4 and (radionuclid? or radiolabel? or label? or radioactiv?)
 L11 0 L4 AND (RADIONUCLID? OR RADIOLABEL? OR LABEL? OR RADIOACTIV?)

| | | |
|----------------------|------------------|---------------|
| => fil hcaplus | | |
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |

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09/763,777. Page 12

| | | |
|--|------------------|---------------|
| FULL ESTIMATED COST | 10.96 | 292.64 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -7.81 |

FILE 'HCAPLUS' ENTERED AT 09:13:48 ON 07 JUL 2003
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FILE COVERS 1907 - 7 Jul 2003 VOL 139 ISS 2
FILE LAST UPDATED: 6 Jul 2003 (20030706/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s thakur m?/au
L12      431 THAKUR M?/AU

=> s l12 and fibrin?
        49229 FIBRIN?
L13      2 L12 AND FIBRIN?

=> d ibib ab 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y
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L13 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:133431 HCAPLUS
 DOCUMENT NUMBER: 132:162909
 TITLE: Imaging with Tc-99m labeled fibrin
 -alpha-chain peptide
 INVENTOR(S): Thakur, Madhukar L.
 PATENT ASSIGNEE(S): Thomas Jefferson University, USA
 SOURCE: PCT Int. Appl., 29 pp.
 CODEN: PIXXDP

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2000009076 | A2 | 20000224 | WO 1999-US19011 | 19990817 |
| WO 2000000076 | A3 | 20000511 | | |
| | W, CA, JP | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | |
| EP 1105164 | A2 | 20010613 | EP 1999-966745 | 19990817 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| PRIORITY APPLN. INFO.: | | | US 1998-96803P | P 19980817 |
| | | | WO 1999-US19011 | W 19990817 |

OTHER SOURCE(S): MARPAT 132:162909

AB The present invention involves compns. for radiolabeled agents for imaging mammalian tissue or cells, compns. for radiolabeling agents that bind to mammalian tissue or cells, compns. for radiolabeling agents that bind to fibrin, and methods of using said compns. Examples are given of deep venous thrombosis and pulmonary embolism scintigraphy using 99mTc-labeled decapeptide Gly-Pro-Arg-Pro-Pro-Aba-Gly-Gly-(D)-Ala-Gly (Aba = 4-aminobutyric acid).

L13 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:80114 HCAPLUS
 DOCUMENT NUMBER: 133:553779
 TITLE: Imaging vascular thrombosis with 99mTc-labeled fibrin alpha-chain peptide
 AUTHOR(S): Thakur, Madhukar L.; Pallela, Venkat R.; Consigny, P. Macke, Rao, Ponugoti S.; Veselova-Belnikovska, Donka; Shi, Ron
 CORPORATE SOURCE: Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, PA, 19107, USA
 SOURCE: Journal of Nuclear Medicine (2000), 41(1), 161-168
 CODEN: JNMAQ; ISSN: 0161-5505
 PUBLISHER: Society of Nuclear Medicine, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB An agent that permits scintigraphic detection of chronic deep venous thrombosis (DVT) or pulmonary embolism (PE) would be a welcome addn. to the armamentarium of nuclear medicine. Because fibrin is the integral part of each clot, old or fresh, we hypothesized that a 99mTc-labeled fibrin alpha-chain N-terminal peptide, Gly-Pro-Arg-Pro-Pro, that binds to the C-terminal portion of the gamma-chain of fibrin can detect DVT and PE. Methods: The peptide was modified to Gly-Pro-Arg-Pro-Pro-Aba-Gly-(D)-Ala-Gly to permit efficient binding of 99mTc (99mTc-TP 850). The stability of the peptide was exampd. in vitro as well as in vivo. The ability of the agent to bind to rabbit, dog, and human fibrin and to inhibit ADP-induced platelet aggregation was exampd. Blood clearance and 3-h tissue distribution were studied. DVT was induced in 8 rabbits using a stimulating electrode and in 2 rabbits by inserting a thrombin-soaked suture. PE was induced in 6 addnl. rabbits by introducing tantalum-impregnated blood clots into the right atrium, and the rabbits were radiographed to locate the emboli. 99mTc-TP 850 was then injected through a lateral ear vein, and each rabbit was imaged for up to 3 h. The rabbits were then killed, the heart and lungs were dissected and radiographed and the clots were harvested so that clot-to-blood radioactivity ratios could be detd. Results: The peptide analog permitted efficient incorporation of 99mTc, which was stable in vitro and in vivo. The blood clearance was biphasic, with an alpha. phase half-life of approx. 4 min (20%) and a beta. phase half-life of approx. 13 min (88%). The mean binding of 99mTc-TP 850 to human, dog, and rabbit fibrin was 46% +/- 2%, 60% +/- 3%, and 56% +/- 2.5%, resp., and the inhibitory concn. of 50% for dog and rabbit platelet aggregation was 236 .mu.m and 167 .mu.m, resp. All clots, including 24-h-old pulmonary emboli, were delineated. The radioactivity assoccd. with clots varied from 0.01 to 0.09 %ID/g, with clot-to-blood radioactivity ratios ranging from 1.2 to 12.0. However, 48-h-old pulmonary emboli had lysed and were seen neither by radioisotopic nor by scintigraphy. Conclusion: A fibrin alpha-chain, N-terminal peptide that binds to the C-terminal portion of the gamma-chain of fibrin has been modified and labeled with 99mTc. The resultant peptide is stable in vitro and in vivo; binds to human, dog, and rabbit fibrin in large quantities; and inhibits platelet aggregation. The peptide clears rapidly from the blood and delineates exptl. DVT and PE in rabbits. This agent is worthy of further investigation.

L13 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2003 ACS (Continued)
 investigation.
 REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT